claim 55 can be found in Example 14 and Figure 6.: support fro new claim 56 can be found at page 12, line 17 – 18.

No new matter is added. A copy of the claims marked up as amended is attached.

Election/Restrictions

Applicants hereby confirm the provisional election made to prosecute the invention of Group III, claims 36-39, drawn to methods for treatment. Applicants expressly reserve the rights to pursue the other claims in a divisional application(s) in the future.

Claim Objections

Claim 37 has been amended to correct the typographical error. Withdrawal of this objection is requested.

Claim Rejection Under 35 U.S.C. §112 ¶2

Claims 36-39 have been rejected under 35 U.S.C. §112 ¶2 as being indefinite. Reference to a canceled claim--claim 20--and the recitation of "geriatric skin" and "precancerous conditions" were called into question. The Examiner considered these two terms not adequately defined in the specification or claim language and, in addition, questioned the reference to "geriatric skin" as a form of disease.

Claim 36 has been amended to delete the reference to claim 20 and to recite "condition" instead of "disease," thereby obviating the dependency problem and the apparent inconsistency between "skin" and "disease." Applicants respectfully submit that "geriatric skin" is adequately defined by its plain meaning. It refers to skin aging, which a skilled artisan would understand to mean reduced skin activity, deterioration of skin, reduction of skin strength, and development of wrinkles and skin cancers. Therefore, the recitation of "geriatric skin" is not indefinite. In further response, however, applicants have amended claim 36 to recite a "geriatric skin condition." With regard to "precancerous conditions," this is a term of art which one of ordinary

skill in the art would readily understand to refer to any conditions or abnormal changes prior to cancerous transformation. The specification provides adequate discussions thereon. See, e.g., Specification, pages 5&6.

Withdrawal of this rejection is accordingly respectfully requested.

Claim Rejection Under 35 U.S.C. §102

Claims 36-39 have been rejected under 35 U.S.C. §102 as being anticipated by each of the three documents cited:

1. Angeli (WO 91/15218). This reference teaches certain therapeutic compositions for treatment of psoriasis which includes extracts from a number of medicinal herbs, including St. John's Wort. It discloses the use of St. John's Wort in the treatment of slight skin disorders and slowly healing wounds. See, Id, page 8.

2. Khan (GB 2311009A). This reference teaches extracts of a number of herbs, with a preferably additional extract from Hypericum perforatum, for treatment of fungal infections of skin lesions. See, Id, Abstract, page 4.

3. Shatkina (US 4911925). This reference teaches a pharmaceutical composition for treatment of skin, particularly aging skin. The composition includes a vegetable extract of Hypericum perforatum L. See, Id., page 3-4.

The Examiner asserted that the claimed methods were inherently practiced by practicing the treatment method of either Angeli, Khan, or Shatkina, because extracts of hypericum perforatum have been known to contain both hyperforin and hypericin.

Applicants respectfully traverse this rejection. As amended, the rejected claims preclude any active ingredients other than those specifically recited. As will be discussed further below, the art shows compositions containing numerous active ingredients in addition to those recited in the claims, as amended. I most cases, the active ingredient is not even disclosed in the references. Thus, the art does not anticipate the claimed invention. Additionally, the methods of claims 36-39 require (i) an effective amount for

treating the enumerated disease conditions and (ii) the application to a subject in need thereof. Neither of these elements is taught by any of the aforementioned references. For example, it is not clear from Angeli which extract is active, or which component within this extract might be pharmacologically active, much less the effective amount of this active component. Shatkina discloses a method to prepare a vegetable extract by introducing 10-20 g of the mixture of the four plants into 200 ml of boiling water and letting the mixture sit for 20 minutes, followed by sieving and further processing (column 2, lines 40-46). However, Shatkina fails to shed light on which component (at which amount) of the extract might have any positive effect on the skin. Likewise, there is no teaching or suggestion in Khan that reveals to the skilled artisan the active composition as claimed and the effective amount thereof for treating the recited disease conditions. Therefore, none of the references anticipates the pending claims.

The art similarly is not applicable to new claims 40-45, which prescribe specific concentrations of hyperforin or hyperforin and hypericin.

Accordingly, applicants respectfully request withdrawal of this rejection.

Claim Rejection Under 35 U.S.C. §103

Claims 36-39 have been rejected under 35 U.S.C. §103 as being obvious in view of the prior art references, citing Khan, Shatkina, and three additional publications, Khwaja (WO 97/39355), Valavichyas (1986) and The Hypericum Home Page (1996). The Examiner asserted that these references, taken together, provided one of ordinary skill in the art the motivation to arrive at the invention.

The Examiner asserts that by practicing the methods of Khan and Shatkina, one would be inherently practicing the claimed invention. Applicants traverse this rejection because inherency cannot support an obviousness rejection. The art must explicitly suggest the claimed invention.

The Examiner further asserts that The Hypericum Home Page teaches that extracts of St. Johns Wort, particularly hypericin demonstrates anti-

cancer properties and has been proven to inhibit tumor cells of the brain, lung and skin. She further asserts that Khwaja teaches that extracts of St. John's Wort include antibacterial, anticancer, antimutagenic and antiviral uses. She further asserts that Valavichyus teaches that extracts of St John's Wort, specifically oil extracts inhhibits growth of sarcoma cells.

Applicants respectfully traverse this rejection for the same reasons discussed above. In particular, the effective amount for treating any of the recited disease conditions is not made apparent from the references read alone or in combination. The Hypericum Home Page is a review article that mentions, in passing, that work has shown hypericin to have promising anti-cancer properties *in vitro*. It provides no further information and mentions only hypericin, rather than hyperforin or hyperforin and hypericin as recited in the claims.

Khwaja relates to many different plant medicines and provides a detailed analysis of each. However, it also does not direct the skilled artisan toward the ingredients or treatments recited in the claims. In fact, Khwaja is more relevant for supporting a finding of non-obviousness. At page 105, Khwaja states that St. John's Wort contains numerous active components and lists them (Paragraph 9.6). It states that "[m]ost researchers consider it's (St. John's Wort) effects to be due to a variety of constituents rather than to any single component." (Page 105, lines 8-10) A chart at page 111 shows activities associated with the various constituents. Although constituents hyperforin and hypericin are listed, so also are adhyperforin, amentoflavone, flavonoids, GABA, Methyl-2-butenol, proanthocyanindins and xanthones. Although an anticarcinogenic use has been noted for St. John's Wort, this use is associated with adhyperforin and not hyperforin. Khwaja 's discussion of St. John's Wort and its varied uses clearly demonstrates that St. John's Wort is a very complex plant and that different parts of the plant provide different concentrations of the various active components. *See e.g.*page 106 and the description of the amount of hypericin content in different plant types and parts.

Valavichyus is a short abstract which mentions that the administration of oil extacts from St. John's Wort and Chamomilla inhibited sarcoma growth in rats. It is not clear from this reference whether the oil extracts were independently tested or whether there was a combination of oils tested. Also, nothing in this reference indicates which active agents were responsible for the results and nothing in this reference teaches or suggests the concentrates recited in the present claims.

Applicants request that the obviousness rejection be withdrawn in view of the above amendments and comments.

CONCLUSION

In view of the forgoing amendments and remarks, applicants await an action on the merits in which the amended claims are considered. The Examiner is invited to contact the undersigned if further discussion should advance prosecution.

Respectfully submitted,

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Marked Copy of Claims as Amended

36. (Amended) A method for treating a [disease] **condition, comprising administering to a subject in need thereof an effective amount of a composition consisting of (a) pharmaceutically acceptable carrier and (b) active agent consisting of (i) hyperforin or (ii) hyperforin and hypericin, wherein said condition is** selected from the group consisting of: cancer; an inflammatory skin [diseases] **condition**; **a** precancerous condition[s]; **a** geriatric skin **condition**; and **a** microbial skin infection[s, comprising administering to a skin of a subject in need thereof an effective amount of a composition according to claim 20].

37. (Amended) The method according to claim 36, wherein the [disease] **condition** is [ecezema] **eczema**.

38. (Amended) The method according to claim 36, wherein said [disease] **condition** is selected from the group consisting of: exsiccation eczemas; hyperkeratotic hand and foot eczemas; contact eczemas; atopic dermatitis; neurodermatitis; lichen simplex; prurigo simplex; lymphomas; leukemia; melanoma; **an** epithelial pre-cancerous condition[s]; tumor metastases; and epithelial tumor.

40. (New) The method according to claim 36, wherein said composition is in the form of a topical ointment and said effective amount consists of at least 15 μg hyperforin per ml.

41. (New) The method according to claim 36, wherein said composition is in the form of a topical ointment and said effective amount is 0.02-20 mg hyperforin per ml.

42. (New) The method according to claim 41 wherein said effective amount is 1-20 mg hyperforin per ml.

43. (New) The method according to claim 42. wherein said effective amount is 10 mg hyperforin per ml.

44 (New) The method according to claim 36, wherein said effective amount is at least 15 μg hypericin per ml.

45. (New) The method according to claim 36, wherein said effective amount of hypericin is 20-150 μg hypericin per ml.

46. (New) A method of treating cancer comprising administering to a subject in need thereof an effective amount of a composition comprising hyperforin and a pharmaceutically acceptable carrier.

47. (New) The method according to claim 46, wherein said effective amount comprises at least 50 μg/ml of hyperforin in a form suitable for injection into a tumor.

48. (New) The method according to claim 46, wherein said effective amount is at least 100 μg hyperforin per μl in a form suitable for epicutaneous application.

49. (New) The method according to claim 46, wherein said effective amount is at least 50 μg hyperforin per ml in plasma when administered systemically.

50. (New) The method of claim 46, wherein said cancer is a melanoma.

51. (New) The method of claim 46, wherein said cancer is a lymphoma.

52. (New) The method of claim 46, wherein said cancer is a skin cancer.

53. (New) The method of claim 46, wherein said cancer is mammary carcinoma.

54. The method of claim 46, wherein said cancer is leukemia carcinoma.

55. (New) A method of inhibiting keratinocyte cell proliferation comprising administering to a subject a cell proliferation inhibiting amount of hyperforin, wherein said amount is at least 100 μg/ml.

56. (New) The method of one of claims 46 or 55, wherein said hyperforin is at least 90% pure.